

What is claimed is:

1. A controlled-release oral dosage formulation of a salt-forming active ingredient, wherein the active ingredient is present as at least two different salts in a solid aggregation state, wherein the two different salts have different water solubility and release the active ingredient *in-vitro* at different release rates, provided that oral dosage formulations are excluded which comprise a resin carrying a sulfonate group and a resin carrying a carboxyl group and which contain an active ingredient in a form fixed to these resins.

2. A controlled-release oral dosage formulation according to claim 1, wherein the water solubilities of the at least two different salts differ from one another at least by a factor of 2.

3. A controlled-release oral dosage formulation according to claim 1, wherein the active ingredient is selected from the group consisting of salt-forming, pharmaceutically active ingredients, vitamins, minerals, nutrients and diagnostic agents.

4. A controlled-release oral dosage formulation according to claim 3, wherein the active ingredient is a salt-forming pharmaceutically active ingredient.

5. A controlled-release oral dosage formulation according to claim 4, wherein the salt-forming pharmaceutical active ingredient is selected from the group consisting of salt-forming analgesics, anthelmintics, anti-arrhythmics, antiasthmatics, antidepressants, antidiabetics, antidotes, antiallergics, antitussives, antibiotics, anti-emetics, anti-infectives, antihistamines, antihypertensives, antihypertensives, antihypotonics, anticoagulants, antirheumatics, antipyretics, anxiolytics, slimming drugs, drugs for treatment of acidosis, drugs for treatment of vertigo, antihæmorrhagics, antifibrinolytics, haemostatics, antihypoglycaemics, antihypotonics, antimycotics, antiphlogistics, expectorants, drugs for treatment of arteriosclerosis, beta-adrenoceptor blockers, calcium-channel blockers, renin-angiotensin inhibitors, broncholytics, cholagogues, biliary tract therapeutics, cholinergics, corticoids for internal administration, circulation-stimulating drugs, detoxification drugs, geriatric drugs, gout treatment drugs, anti-influenza drugs, cold treatment drugs, gynaecological drugs, hepatic drugs, hypnotics, pituitary gland hormones, hypothalamic hormones, regulatory peptides, regulatory peptide inhibitors, immunomodulators, cardiac drugs, analeptics,

antihypoxaemics, antianaemics, antimentia drugs, nootropics, appetite suppressants, coronary drugs, laxatives, chemotherapeutics, diuretics, enzymes, fungistatics, hormones, lipid-lowering drugs, neural therapeutics, gastrointestinal drugs, anti-migraine drugs, mineral preparations, muscle relaxants, anti-neuropathy drugs, neurotropic drugs, neuroleptics, drugs for treatment of osteoporosis, calcium metabolism regulators, anti-parkinsonian drugs, drugs for treatment of extrapyramidal symptoms, psychoactive drugs, roborants, tonics, thyroid therapeutics, sex hormones, sex hormone inhibitors, spasmolytics, thrombocyte aggregation inhibitors, anti-tuberculosis drugs, urologics, vein-therapeutics, antineoplastic drugs or protectives, muscle relaxants, psychoactive drugs, sedatives, spasmolytics, vasodilators, virustatics and cytostatics.

6. A controlled-release oral dosage formulation according to claim 4, wherein the active ingredient is selected from the group consisting of analgesics, anti-infectives and neuroleptics.

7. A controlled-release oral dosage formulation according to claim 6, wherein the analgesic is selected from the group consisting of salt-forming opioids, compounds with opioid action and non-steroidal analgesics.

8. A controlled-release oral dosage formulation according to claim 7, wherein the analgesic is selected from the group consisting of brifentanil, carfentanil, fentanyl, lofentanil, ocfentanil, trefentanil, codeine, dextropropoxyphene, dihydrocodeine, diphenoxylate, meptazinol, nalbuphine, pethidine, meperidine, tilidine, tramadol, viminol, butorphanol, dextromoramide, dezocine, diacetylmorphine, heroin, hydrocodone, hydromorphone, ketobemidone, levomethadone, levomethadyl, levorphanol, morphine, nalorphine, oxycodone, pentazocine, piritramide, alfentanil, buprenorphine, etorphine, fentanyl, remifentanyl and sufentanyl.

9. A controlled-release oral dosage formulation according to claim 8, wherein the analgesic is tramadol or morphine.

10. A controlled-release oral dosage formulation according to claim 5, wherein the salt-forming neuroleptic is promethazine.

11. A controlled-release oral dosage formulation according to claim 1, wherein the active ingredient salt is selected from the group consisting of chloride, bromide, sulfate, sulfonate, phosphate, tartrate, theoclate, embonate, formate, acetate, propionate, benzoate, oxalate, succinate, citrate, diclofenacate, naproxenate, salicylate,

acetylsalicylate, glutamate, fumarate, aspartate, glutarate, stearate, butyrate, malonate, lactate, mesylate, saccharinate, cyclamate and acesulfamate salt.

12. A controlled-release oral dosage formulation according to claim 11, wherein the active ingredient salt is a chloride, sulfate, saccharinate, theoclate, embonate, diclofenacate, naproxenate or salicylate salt.

13. A controlled-release oral dosage formulation according to claim 1, wherein the active ingredient salt is an alkali metal salt, alkaline-earth metal salt, ammonium salt, iron salt or aluminum salt.

14. A controlled-release oral dosage formulation according to claim 13, wherein the active ingredient salt is a sodium or potassium salt.

15. A controlled-release oral dosage formulation according to claim 1, wherein the dosage formulation is tablets, chewable tablets, chewing gums, coated tablets, or powders.

16. A controlled-release oral dosage formulation according to claim 15, wherein the dosage formulation is filled into capsules.

17. A controlled-release oral dosage formulation according to claim 1, wherein the dosage formulation is tablets.

18. A controlled-release oral dosage formulation according to claim 1, wherein the dosage formulation is in multi-particulate form.

19. A controlled-release oral dosage formulation according to claim 18, wherein the dosage formulation is in the form of microparticles, micro-tablets, microcapsules, granulates, active-substance crystals or pellets.

20. A controlled-release oral dosage formulation according to claim 19, wherein the dosage formulation is in the form of micro-tablets, granulates or pellets.

21. A controlled-release oral dosage formulation according to claim 18, wherein the dosage formulation is filled into capsules or compressed into tablets.

22. A controlled-release oral dosage formulation according to claim 20, wherein the granulates or pellets have a size within the range of 0.1 to 3 mm.

23. A controlled-release oral dosage formulation according to claim 22, wherein the granulates or pellets have a size within the range of 0.5 to 2 mm.

24. A controlled-release oral dosage formulation according to claim 19, wherein the micro-tablets have a diameter of 0.5 to 5 mm.

25. A controlled-release oral dosage formulation according to claim 24, wherein the micro-tablets have a diameter of 1 to 3 mm.

26. A controlled-release oral dosage formulation according to claim 25, wherein the micro-tablets have a diameter 1 to 2 mm.

27. A controlled-release oral dosage formulation according to claim 19, wherein the active-substance crystals, micro-particles, micro-pellets or micro-capsules have a diameter of 10 μm to 1 mm.

28. A controlled-release oral dosage formulation according to claim 27, wherein the active-substance crystals, micro-particles, micro-pellets or micro-capsules have a diameter of 15 μm to 0.5 mm.

29. A controlled-release oral dosage formulation according to claim 28, wherein the active-substance crystals, micro-particles, micro-pellets or micro-capsules have a diameter of 30 μm to 200 μm .

30. A controlled-release oral dosage formulation according to claim 1, wherein at least one of the at least two salts of the active ingredient is in a sustained-release formulation.

31. A controlled-release oral dosage formulation according to claim 30, wherein all of the salts of the active ingredient are in a sustained-release formulation.

32. A controlled-release oral dosage formulation according to claim 30, wherein the sustained-release formulation is achieved by a retarding coating, or by embedding the active ingredient in a retarding matrix, or both.

33. A controlled-release oral dosage formulation according to claim 30, wherein the retarding coating is based on (1) a water-insoluble, modified, natural or synthetic polymer, (2) natural, semi-synthetic or synthetic wax, (3) natural, semi-synthetic or synthetic fat, (3) natural, semi-synthetic or synthetic fatty alcohol, or (4) a mixture of at least two of (1), (2) and (3).

34. A controlled-release oral dosage formulation according to claim 33, wherein the retarding coating further comprises a conventional softener.

35. A controlled-release oral dosage formulation according to claim 33, wherein the water-insoluble polymer is a poly(meth)acrylate, a poly(meth)acrylate copolymer, or a mixture thereof.

36. A controlled-release oral dosage formulation according to claim 35, wherein the poly(meth)acrylate is poly(C₁₋₄)-alkyl(meth)acrylate or poly(C₁₋₄)-dialkylamino-(C₁₋₄)-alkyl(meth)acrylate.

37. A controlled-release oral dosage formulation according to claim 35, wherein the poly(meth)acrylate copolymer is ethylacrylate/methylmethacrylate-copolymer with a molar ratio of the monomers of 2:1, ethylacrylate/methylmethacrylate/trimethylammonium ethylmethacrylate-chloride-copolymer with a molar ratio of the monomers of 1:2:0.1, or ethylacrylate/methylmethacrylate/trimethylammonium ethylmethacrylate-chloride-copolymer with a molar ratio of the monomers of 1:2:0.2.

38. A controlled-release oral dosage formulation according to claim 33, wherein the water-insoluble polymer is a cellulose derivative.

39. A controlled-release oral dosage formulation according to claim 38, wherein the cellulose derivative is alkyl cellulose or cellulose ester.

40. A controlled-release oral dosage formulation according to claim 39 wherein the alkyl cellulose is ethyl cellulose.

41. A controlled-release oral dosage formulation according to claim 39, wherein the cellulose ester is cellulose acetate

42. A controlled-release oral dosage formulation according to claim 35, wherein the water-insoluble polymer is applied from an aqueous medium

43. A controlled-release oral dosage formulation according to claim 42, wherein the aqueous medium is aqueous latex or pseudo-latex dispersion.

44. A controlled-release oral dosage formulation according to claim 33, wherein the water-insoluble polymer is a mixture of polyvinyl acetate and polyvinyl pyrrolidone.

45. A controlled-release oral dosage formulation according to claim 44, wherein the mixture of polyvinyl acetate and polyvinyl pyrrolidone is in the form of an aqueous pseudo-latex dispersion.

46. A controlled-release oral dosage formulation according to claim 33, wherein the retarding coating is based on carnauba wax, beeswax, glycerine monostearate, glycerine monobehenate, glycerine ditripalmitostearate, or microcrystalline wax, or a mixture of at least two thereof.

47. A controlled-release oral dosage formulation according to claim 35, wherein the coating material further comprises a conventional softener.

48. A controlled-release oral dosage formulation according to claim 47, wherein the conventional softener is selected from the group consisting of a lipophilic diester of a C₆-C₄₀ aliphatic or aromatic dicarboxylic acid and a C₁-C₈ aliphatic alcohol, a hydrophilic or lipophilic ester of citric acid, a polyethylene glycol, a propylene glycol, an ester of glycerine, oleic acid or a mixture of at least two thereof.

49. A controlled-release oral dosage formulation according to claim 48, wherein the lipophilic diester of a C₆-C₄₀ aliphatic or aromatic dicarboxylic acid and a C₁-C₈ aliphatic alcohol is dibutylphthalate, diethylphthalate, dibutyl sebacate or diethyl sebacate.

50. A controlled-release oral dosage formulation according to claim 48, wherein the hydrophilic or lipophilic ester of citric acid is triethyl citrate, tributyl citrate, acetyltributyl citrate or acetyltriethyl citrate.

51. A controlled-release oral dosage formulation according to claim 48, wherein the ester of glycerine is triacetin, an acetylated mono- and diglyceride or a mid-chain triglyceride.

52. A controlled-release oral dosage formulation according to claim 47, wherein the softener is present in quantities of 5 to 50 wt.% relative to the polymer coating material.

53. A controlled-release oral dosage formulation according to claim 52, wherein the softener is present in quantities of 10 to 40 wt.% relative to the polymer coating material.

54. A controlled-release oral dosage formulation according to claim 53, wherein the softener is present in quantities of 10 to 30 wt.% relative to the polymer coating material.

55. A controlled-release oral dosage formulation according to claim 32, wherein the retarding matrix is based upon a hydrophilic matrix material.

56. A controlled-release oral dosage formulation according to claim 55, wherein the hydrophilic material is a hydrophilic polymer.

57. A controlled-release oral dosage formulation according to claim 56, wherein the hydrophilic polymer is at least one of the group consisting of a cellulose ether, a cellulose ester and acrylic resins.

58. A controlled-release oral dosage formulation according to claim 57, wherein the hydrophilic polymer is at least one selected from the group consisting of ethyl cellulose, hydroxypropylmethyl cellulose, hydroxypropyl cellulose, hydroxymethyl cellulose, poly(meth)acrylic acid and their salts, amides and esters.

59. A controlled-release oral dosage formulation according to claim 32, wherein the coating matrix is based on a hydrophobic matrix material

60. A controlled-release oral dosage formulation according to claim 59, wherein the hydrophobic material is selected from the group consisting of hydrophobic polymers, waxes, fats, long-chained fatty acids, their corresponding esters, their corresponding ethers, and their mixtures.

61. A controlled-release oral dosage formulation according to claim 60, wherein the hydrophobic material is selected from the group consisting of mono- or diglycerides of C₁₂-C₃₀ fatty acids, C₁₂-C₃₀ fatty alcohols, waxes and mixtures thereof.

62. A controlled-release oral dosage formulation according to claim 1, further comprising a protective coating.

63. A controlled-release oral dosage formulation according to claim 62, wherein the protective coating is a gastric juice-resistant protective coating.

64. A controlled-release oral dosage formulation according to claim 63, wherein the gastric juice-resistant coating comprises a methacrylic acid/methylmethacrylate copolymer with a molar ratio of the monomers of 1:1, a

methacrylic acid/methylmethacrylate copolymer with a molar ratio of the monomers of 1:2, a methacrylic acid/ethylacrylate copolymer with a molar ratio of the monomers of 1:1, a methacrylic acid/methylacrylate/ methylmethacrylate with a molar relationship of the monomers of 7:3:1, shellac, hydroxypropylmethyl cellulose acetate succinate, and cellulose acetate phthalate, or a mixture of at least two thereof.

65. A controlled-release oral dosage formulation according to claim 64, wherein the gastric juice-resistant coating further comprises a poly(meth)acrylate.

66. A controlled-release oral dosage formulation according to claim 65, wherein the poly(meth)acrylate is at least one of the group consisting of an ethylacrylate/methylmethacrylate-copolymer with a molar ratio of the monomers of 2:1, an ethylacrylate/methylmethacrylate/trimethylammonium ethylmethacrylate-chloride-copolymer with a molar ratio of the monomers of 1:2:0.1, or an ethylacrylate/methylmethacrylate/trimethylammonium ethylmethacrylate-chloride-copolymer with a molar ratio of the monomers of 1:2:0.2.

67. A controlled-release oral dosage formulation according to claim 1, the formulation is prepared by a process comprising producing a mixture by mixing at least two different salts of the active ingredient, the salts having a different in-vitro release rate, formulating the mixture, and coating the mixture with a protective coating.